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STATUS OF VITAMIN E IN TREATMENT OF HEART DISEASE

During the past three years widespread discussion has arisen concerning the uses of vitamin E in clinical medicine. Vitamin E is not a new product or discovery. Its existence has been known for at least twenty-five years, and it has been used extensively for various gynecological and endocrinological disorders for two decades. In 1946 and 1947, Vogelsang, Shute and Shute[1] published a series of articles enthusiastically describing the benefits to be obtained from the use of vitamin E in a number of cardiac conditions. They claimed improvement in the great majority of patients with congestive failure, myocardial infarction, angina pectoris, hypertensive heart disease and rheumatic fever. The extensive publicity which these reports received in the lay press and in the advertising literature of some pharmaceutical manufacturers stimulated great interest in this supposed cardiac panacea. The above workers and others have extended these observations and have recommended vitamin E also for gangrene of the extremities, Buerger's disease, certain skin disorders, muscle dystrophies, arthritis and diabetes mellitus.

Subsequent independent investigations, however, have failed to confirm the value of vitamin E therapy in heart disease. We thought it would be of benefit, therefore, to review some of the experimental and clinical data that have been published.

Vitamin E is a mixture of alpha, beta, gamma and delta tocopherols. The tocopherols are widely distributed in nature, being found particularly in vegetable oils and green leaves. The therapeutic effects in cardiac and other disorders have been attributed principally to the alpha tocopherols.

An extensive literature has accumulated describing the effects of vitamin E deprivation in various experimental animals[2]. Myocardial scarring and pigment changes in heart muscle were reported in animals kept on vitamin E deficient diets for long periods of time. Cardiac enlargement was observed and electrocardiographic abnormalities were reported. Necropsy studies of cattle dying with vitamin E deficiency revealed cardiac failure and microscopic lesions in the heart similar to those seen in rheumatic disease in humans. The results of all these investigations, however, have not been confirmed by independent workers. Also, there have been variations in different species of animals studied. Even accepting the validity of these observations, their relation to the problem of heart disease in the human is uncertain. We know very little about the metabolism of vitamin E in human beings. Methods for measuring the tissue content and intermediary metabolism of vitamin E are still quite experimental. In fact, it is not known whether vitamin E deficiency actually occurs in man. The demonstration of cardiac abnormalities in vitamin E deficient animals is therefore a rather uncertain basis for recommending the use of vitamin E in the treatment of human heart disease. It would appear just as illogical to prescribe thiamin chloride or thyroid for most patients with heart disease because prolonged deprivation of these agents may be associated with clinical, electrocardiographic or pathological changes in the heart.

The recommended daily dose of 200 mgms. or more of alpha tocopherol considerably exceeds that necessary to correct a deficiency. Actually, the advocates of vitamin E therapy in heart disease have not claimed that their results were due to correction of a deficiency, but have attributed them to some unidentified pharmacological action. Dilatation of small blood vessels and alteration of intracellular oxidation have been suggested as mechanisms, but the proof has not been too convincing.

It does not appear likely that one agent would affect such diverse conditions as acute rheumatic fever, coronary insufficiency and congestive failure. A review of the papers attesting to the beneficial effects of vitamin E hardly leads to the enthusiasm exhibited by the authors. Noteworthy is the uncritical manner in which the cases are presented, particularly the failure to take into account the natural history of the cardiac disturbance under consideration. Cases are tabulated demonstrating the success of vitamin E therapy, whereas the abstract itself indicates that the improvement was due to digitalis. The changing electrocardiographic picture in acute myocardial infarction and acute rheumatic fever is attributed to the use of vitamin E, when it may be a natural occurrence. Credit for freedom from pain after the first few hours or days of acute myocardial infarction is given to vitamin E, when this could well be the normal course of the disease.

We shall limit our remaining comments to a consideration of some of the clinical experiences with vitamin E in heart disease that have been reported. Other workers have not been able to duplicate the successes of Vogelsang, Shute and Shute. Makinson, Oleesky and Stone[3] treated twenty-two patients with angina pectoris successively with alpha tocopherol, phenobarbital, aminophylline and as a control, calcium lactate. They concluded that vitamin E was no more efficacious than aminophylline or phenobarbital and that none were of much value. Ball[4] studied ten patients with angina pectoris and could consider only one as definitely improved after six weeks of vitamin E therapy. Gram and Schmidt[5] found definite improvement in only five of eighty patients with cardiac disease who were treated with vitamin E.

Levy and Boas[6] studied thirteen patients treated with vitamin E and concluded that "there was no evidence of diuresis or amelioration of the symptoms or signs of chronic heart failure in the five cases studied. Nor was there any evidence whatsoever that this drug affected the pattern, the frequency, the intensity, or the precipitation of anginal pain, in five cases of anginal pain with a stable pattern of chest pain related to effort. Likewise in three cases of active angina pectoris characterized by a new pattern of increased frequency and intensity of attacks often occurring at complete rest, there was no change to be attributed to the use of this vitamin."

Ravin and Katz[7] studied eleven patients with angina pectoris by the two-step exercise tolerance test. In only one case was there any difference between the performance before and after treatment with vitamin E and in this case the consumption of nitroglycerine had increased markedly in the month during which the patient was followed. Five other patients taking nitroglycerine exhibited no significant change in the number of tablets required. In only one case was there slight subjective improvement, but there was no improvement in the performance of the two-step test.

Donegan[8], et al, studied twenty-one patients (seven with hypertensive heart disease, seven with hypertension, and seven with classical stable angina pectoris) treated alternately with placebos and tocopherols. No appreciable benefit either subjectively or objectively was noted.

The results of our[9] study were likewise disappointing. Definite improvement was not noted in any of eleven patients with congestive failure, five patients with angina pectoris and six patients with hypertensive and/or arteriosclerotic heart disease. When subjective improvement occurred in a few patients, the effect could be duplicated by a placebo. When patients with congestive failure were receiving vitamin E and the attempt was made to withhold their digitalis or mercurial diuretics, aggravation or recurrence of the manifestations of failure promptly ensued. Significant alterations in blood pressure or in the appearance of electrocardiograms and orthodiagrams were not noted.

The complete lack of successful or even promising results reported by so many investigators leads to the conclusion that the value of vitamin E in the treatment of heart disease has not been proven.

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ANNUAL MEETING

The Annual Meeting and Twenty-Third Scientific Session of the American Heart Association will be held at the Fairmont Hotel, San Francisco, June 22-25, 1950. All those desiring to attend should make room reservations at the earliest possible date.

PROGRAM COMMITTEE

The Chairman of the Program Committee for the Annual Scientific Session is Doctor Louis E. Martin, 1136 West Sixth Street, Los Angeles 14, California. All who desire to present papers at the meetings in San Francisco should forward to Doctor Martin an abstract (in triplicate) of the proposed presentation of not more than 300 words. The deadline for the receipt of abstracts is March 1, 1950.

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